

The KIDROP model of combining strategies for providing retinopathy of prematurity screening in underserved areas in India using wide-field imaging, tele-medicine, non-physician graders and smart phone reporting

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Aim: To report the Karnataka Internet Assisted Diagnosis of Retinopathy of Prematurity (KIDROP) program for retinopathy of prematurity (ROP) screening in underserved rural areas using an indigenously developed tele-ROP model. **Materials and Methods:** KIDROP currently provides ROP screening and treatment services in three zones and 81 neonatal units in Karnataka, India. Technicians were trained to use a portable Retcam Shuttle (Clarity, USA) and validated against ROP experts performing indirect ophthalmoscopy. An indigenously developed 20-point score (STAT score) graded their ability (Level I to III) to image and decide follow-up based on a three-way algorithm. Images were also uploaded on a secure tele-ROP platform and accessed and reported by remote experts on their smart phones (iPhone, Apple). **Results:** 6339 imaging sessions of 1601 infants were analyzed. A level III technician agreed with 94.3% of all expert decisions. The sensitivity, specificity, positive predictive value and negative predictive value for treatment grade disease were 95.7, 93.2, 81.5 and 98.6 respectively. The kappa for technicians to decide discharge of babies was 0.94 ($P < 0.001$). Only 0.4% of infants needing treatment were missed. The kappa agreement of experts reporting on the iPhone *vs* Retcam for treatment requiring and mild ROP were 0.96 and 0.94 ($P < 0.001$) respectively. **Conclusions:** This is the first and largest real-world program to employ accredited non-physicians to grade and report ROP. The KIDROP tele-ROP model demonstrates that ROP services can be delivered to the outreach despite lack of specialists and may be useful in other middle-income countries with similar demographics.

Key words: Infant blindness, iPhone, middle-income countries, non-physician graders, Retcam, retinopathy of prematurity (ROP), rural areas, screening, smart phones, telemedicine, tele-ophthalmology, tele-ROP, wide-field digital imaging

Retinopathy of prematurity (ROP) is a leading cause of childhood blindness the world-over.^[1] ROP is a disease of the retina that affects preterm, low birth weight infants and has the potential to cause permanent and irreversible blindness, fortunately which is largely preventable.

Retinopathy of prematurity is a major public health problem. India, like other middle-income countries is experiencing the 'third epidemic' of blindness due to ROP^[1,2] and is the country with the highest number of preterm births i.e. 3.5 million annually.^[3] Of the 27 million live-births, approximately 9% are born below 2000 grams,^[4] the potential 'at-risk' population for ROP.^[2,5] However, there are considerable challenges to controlling ROP in India, on account of the increasing provision of neonatal intensive care services with improving neonatal

survival, lack of quality neonatal services, lack of awareness even among care-givers, and inadequately trained man-power for screening and treating ROP, most of whom are located in the large cities. An additional factor is that heavier, more mature infants are also at risk of severe ROP in middle-income countries, including India, which increases the number to be screened. We have recently reported that ROP also affects infants cared for in smaller, rural locations, exploding the myth that it is restricted to tertiary care urban centers.^[7-9] A region-specific strategy is required which addresses these complexities, and an on-going endeavor in India is summarized in this manuscript.^[9-21]

K.I.D.R.O.P. - Karnataka Internet Assisted Diagnosis of Retinopathy of Pre-maturity was initiated in 2007 to address the problems of unscreened rural and semi-urban premature infants for ROP, using a novel platform of telemedicine and employing for the first time, non-physician graders who travel to remote neonatal intensive care units (NICUs). They use a portable wide-field retinal digital camera (Retcam Shuttle, Clarity MSI, CA, USA) to take retinal images which they grade and interpret and make management decisions while in the NICU (i.e. discharge; screen again and when; urgent referral to an ophthalmologist required).^[2,12,16-18] Images captured by the graders are also uploaded and read on the smart phones of ROP specialists in the city or elsewhere on a customized 'Tele-ROP app' and platform (iPhone app, "iCare-TeleOphthalmology" i2i Tele-solutions, Bangalore, India).^[9,19-21]

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This manuscript presents a comprehensive report of several aspects of the program including the working methodology, validation results of technicians to diagnose and decide follow-up, a score for technician training and accreditation, validating smart phone reporting for ROP images and summarizes the lessons learnt in the past six years.

Materials and Methods

K.I.D.R.O.P. currently provides ROP screening for 81 neonatal intensive care units (NICU's) across 18 districts of Karnataka State in Southern India. There are 3 dedicated teams ('Team A's') and 12 'Team B's' for 12 of the district headquarters who were trained and validated in Bangalore. The program was initiated by Narayana Nethralaya Postgraduate Institute of Ophthalmology (NNPIO), Bangalore as a stand-alone program, initially as a pilot for 6 districts in 2008. The NNPIO has undertaken all the training and validation studies.

The program has expanded as a 'public private partnership' under the aegis of the National Rural Health Mission, Ministry of Health and Family Welfare, Government of Karnataka (since 2009). All images, data and reports analyzed in this manuscript are restricted to the 6 districts not covered under the PPP and owned by NNPIO. The Institution Review Board, the Research Committee and the Ethics Committee of NNPIO have approved this program.

Team composition and role

A 'Team A' comprises a project manager, one or two trained and validated technician (s), a driver and a vehicle. Each team is equipped with a Retcam Shuttle (Clarity MSI, USA), a portable laser (532nm green) with laser indirect ophthalmoscopy (LIO) delivery, a laptop with data connectivity, Tele-Care software (i2i Telesolutions, Bangalore, India) and consumables. Each team travels on a fixed schedule on a weekly time-table, visiting the same NICU at a fixed time on a fixed day each week within a radius of approximately 300 kms from their respective headquarters. Overnight accommodation is arranged at the headquarters or adjoining districts depending on the distance and logistics. On an average, 1200-1600 kms are travelled each week and an average of 16-28 NICU's visited by a single team weekly. Besides these scheduled centers, there are NICU's who have a smaller case load and are visited on an 'on-call' basis. The project manager's responsibilities include scheduling infants, reminding mothers, recording and analyzing data obtained during imaging sessions. We have evolved a novel, low-cost method of recruiting infants from centers where the team does not routinely visit.^[10] The manager also plays a vital role of being the liaison between the ROP expert and the neonatologist or pediatrician, the resident doctors, nurses and mothers, especially in promoting recruitment and reducing follow-up attrition. 'B teams' are from the local districts, trained by KIDROP and are not the subject of this manuscript.

Imaging protocol

At each session, technicians perform a modified PHOTO-ROP group^[22,23] imaging sequence to include 7 (minimum) images per eye i.e. dilated anterior segment (obtained without any lens by inverting the Retcam camera). The other six images are obtained using the 130°(ROP lens) provided by the manufacturer and include - macula center, disc center, temporal, superior, nasal and inferior quadrants. Additional images of pathology are obtained at the discretion of the technician. All images are

captured in video mode and relevant stills are saved in the database. All images are obtained in the NICU, the step down room or the eye office under topical anesthesia (Proparacain, 0.5%) complying with standard guidelines.^[16]

Training, validation and accreditation of technicians: (The "STAT" score)

Training and validating a technician is germane to the KIDROP program. We have evolved a training methodology with a scoring system, which we use to accredit a novice technician through levels of expertise [Table 1]. This has resulted from the collective experience of training several private and government teams and is called the "KIDROP STAT" (Score for Training and Accreditation of Technicians) and comprises 3 levels (Level I, II and III) in a 20 point score. The scored parameters include basic knowledge of the disease and the program (1-3), imaging related (4-13), which scores the ability of the technician to obtain well focused, oriented images in a proper sequence which includes the temporal ora or at least zone 3, and speed of acquisition. Image grading and reporting (14-16) relate to his or her ability to diagnose and make a clinical management decision. Decision triage is performed using a template created by KIDROP and includes a 3-way triage using images from both eyes [Table 2]: RED - (Type 1 ROP or serious disease in one or both eyes probably needing treatment or at least urgent evaluation by the expert), ORANGE (Type 2 ROP in at least one eye where follow up is needed; and GREEN (can be discharged). Post imaging (17-19) parameters test the ability of the technician to upload the images, use the Tele-Care software, record the details and aid the project manager in scheduling subsequent follow-up visits using images to educate the mothers. The last parameter on the score is management of complications (20) and is assessed for level II and III technicians.

The 'levels' in the STAT score are created to be water-tight compartments rather than an 'across-the-board' point system used in other scoring systems.^[24] This ensures stricter entry criteria into each level, necessitating all tasks to be completed before accreditation. For example, to qualify as level I, simply having good knowledge of the program and data management will not suffice, if the technician possesses poor skill of image capture or grading and vice-versa. Furthermore, as the expertise increases, speed must improve (6 minutes to 2 minutes per eye), grading scores must improve (60 to >90%), and the number of routine uploads must decrease from all images to only RED's. This ensures that once a technician reaches Level III, he or she is required to upload only images of RED infants, so that the decision of referral can be verified by an expert. Objective scores are obtained for parameters described in 5,6,7,12,16 and 19. Other parameters are assessed using pre and post-tests, theory and practical 'live' assessments. In our program it takes approximately 30 working days to 'create' a Level I and 90 days for a Level III technician. Trainees progress from observation and practicing on a mannequin (Retcam Imaging Practice Kit (Clarity MSI, USA) to live sessions first under supervision and then independently until they are adept in image acquisition and decision making.

Software and smart phones

Images obtained during the session are also uploaded using the TeleCare Software (i2i Telesolutions and Telemedicine Pvt. Ltd, Bangalore). This uploading template is installed on

Table 1: KIDROP's Score for training and accreditation of technicians (copyright)

Parameters	Level 1	Level 2	Level 3
Basics (1-3)			
1. Knowledge	Basic knowledge of: 1) ROP 2) Outreach activity 3) Rules & responsibilities 4) Retcam parts	1) Details of all equipment 2) Stakeholders (Other doctors, administrators) 3) Other common conditions (non-ROP)	1) Comprehensive knowledge of all aspects including regional resource persons 2) Can recognize common pediatric retinal conditions
2. Logistics – Base Hospital	Understands basic checklists	Handles transportation logistics	Comprehensive care of equipment, & improvisation during travel emergency
3. Logistics – On Site	Can perform basic sequence of events: setting up, wrapping baby, analgesia, use of speculum	Can also perform basic monitoring of baby	Can handle all situations including performing scleral depression
Procedure related (4-13)			
4. Patient record	Creates records on software. Calculation of corrected age.	Can source data from staff or local doctor as well	Can source information from site hospital even when missing
5. Quality of image	Minimum of 70% of images in focus	70%- 90% in focus	>90% in focus
6. Orientation	Minimum of 70% of images are oriented to represent the correct quadrant/aspect	70%- 90% oriented	>90% oriented
7. Quadrants	All quadrants plus temporal ora serrata in 60% of cases	Ora serrata in 75% of cases	Ora serrata >75% of cases
8. Illumination	Can work at fixed illumination	Capable of dynamic changes in illumination	Adept at changing illumination as pathology demands
9. Dynamic focus	Sometimes, with difficulty	Can do in most cases	Adept, including raised lesions and peripheral scars
10. Image capture	Accomplishes video mode with difficulty	Comfortably selects stills from video	Adept at image capture & post processing on software
11. Lenses	Can use ROP lens (130)	Can use high magnification with some difficulty	Can use all lenses equally well
12. Speed	Completes one eye (speculum on to off) in ≤ 6 minutes	Completes one eye (speculum on to off) in ≤ 4 min	Completes one eye (speculum on to off) in ≤ 2 min
13. Post image capture	Cannot do image processing	Can do in some cases	Adept at highlighting features
Image Grading and Reporting (14-16)			
14. Disease severity	Can differentiate severe from mild ROP (plus, zone 1, stage 3)	Can diagnose all stages in all zones and recognize pre plus	Adept at diagnosing all forms of the disease including APROP
15. Disease progression	Can compare between visits	Can compare between visits/ eyes/other patients	Can expertly monitor progression or regression of the disease based on the images
16. Decision tree	Will upload all red, all orange and most green Will have minimum 60% accuracy	1) Will upload all red and most orange grades 2) Accuracy minimum 80%	1) Will upload only red. 2) Accuracy >90%
Post-Procedure (17-19)			
17. IT & Image handling	Working knowledge of the tele-ROP software	1) Comfortable with software 2) Understands priority of uploads	1) Exporting formats 2) Report collection and computation 3) Troubleshooting
18. Records	1) Mother card filling 2) Hard and soft copy registers	Online data maintenance	All aspects of records including reports and tabulation

Contd...

Table 1: Contd...

Parameters	Level 1	Level 2	Level 3
19. Follow-up	1) Scheduling appointments – helps project manager 2) Follow-up score min 60% compliance	Successful follow-up score minimum 70%	Successful follow-up score minimum 80%
Complications Management(20)			
20. Complications smangement	Not applicable	Minor aspects of equipment breakdown Parent queries in difficult situations	Can handle sick children, procedure related complications independently, parents queries, equipment breakdown

STAT: Score for Training and Accreditation of Technicians

Table 2: Decision Aiding Algorithm ('Red-Orange-Green Triage') developed by KIDROP

		Findings in the other eye				
		Mature vessels	Regressing ROP	Immature retina	Stage 1 ROP, no plus in non-zone 1 location	Stage 2 with no plus in non-zone 1 location
Findings in one eye	Mature vessels					
	Regressing ROP					
	Immature retina					
	Stage 1 ROP, no plus in non-zone 1 location					
	Stage 2 with no plus in non-zone 1 location					
	Plus or pre plus with any stage any zone					
	Zone 1 disease (any stage)					
	Aggressive posterior ROP					

Green: Discharge; Orange: Follow-up; Red: Referral to ROP Specialist / Needs treatment

another laptop (non Retcam laptop) with internet connectivity via a USB Data card. Images are transferred from the Retcam laptop onto this device using a new CD each time or through a wired LAN connection. Technicians upload images on this customized platform. The software employs patented lossless technology, which is agnostic to the format of the incoming image (MLX, DICOM, PNG or JPEG), allowing universality. The priority of upload is Red > Orange > Green which depends on the level of the technician [Tables 1 and 2]. Increasing expertise would shift it to the left. Following upload, images are available on a virtual work list for the remote expert to read and report. The reporting template uses the International Classification of Retinopathy of Prematurity (ICROP) classification^[25] and Early Treatment for Retinopathy of Prematurity (ETROP) grade^[26] for treatment in a 'drop-down menu' for rapid 'click'. On submission, the report 'reaches' the

same cloud server hosting the data, becoming an integral part of the patient file for access, comparison, printing, sharing, data mining and data analysis in the future. Since November 2009, the ROP expert has been performing the same tasks of viewing and reporting on the iPhone (Apple Inc, Cupertino, USA). A validation of image quality on the iPhone vs on the Retcam Shuttle was performed before using it as the primary mode of reporting. Ten diagnoses were tested for agreement, namely (no ROP, stage 1, 2, or 3, aggressive posterior ROP, zone 1, 2, 3, pre plus and plus disease). Through the program iPhone 3GS, 4S and 5 have been used interchangeably by the reporting expert.

Tracking and follow-up

Every session is recorded in a special ROP register that is maintained in the NICU. the project manager keeps a hard copy.

Each NICU has access to its own data (and none other) through this register. 'ROP cards' record the findings using the ICROP classification^[25] and the date and venue of the next follow-up is indicated, should the mother find another KIDROP center closer for follow-up. We make heavy use of mobile phones to contact the mothers via voice and text messages to remind them about the appointment in advance and if an appointment has been missed.^[9,10]

Treatment

Laser photoablation is the primary modality of treatment and is performed using ETROP recommendations^[26] using 532nm green laser delivered by indirect ophthalmoscopy using standard guidelines. The top surface of the Retcam shuttle, without the laptop, is used to position the infant during treatment. Laser treatment is performed by KIDROP experts who visit the peripheral center, obviating the need for the infant to travel to the city.^[9,15,16,27] When not possible, travel costs to Bangalore are reimbursed.

Data analysis

Data were analyzed using SPSS (Version 17.0). Analysis included the agreement and correlation indices between the technician and ROP expert to diagnose and record follow up. This was compared between records of the ROP expert performing peripheral scleral depression with indirect ophthalmoscopy and comparing it with the technician's judgment recorded after each session using dynamic video assessment of his or her own recording. Both were masked to each other's records. Further, we analyzed agreement and correlation indices between the experts reporting on the iPhone vs on the primary Retcam laptop. The expert had access to the birth weight, gestational and post menstrual age at image capture, to allow a 'real world' experience during reporting. Other demographic details that could identify the patient or session were cropped or deleted. Ten percent of the images were repeated to allow inter-observer variability comparison.

Results

Demographics and distribution

At the time of submission, 3 KIDROP 'A teams' servicing 81 enrolled NICU's in 18 districts in Karnataka have performed 41,237 imaging sessions (babies). Of these, 8503 sessions were performed during 2008-2009 and 22,596 performed during 2011-2102. Sessions for analysis of this manuscript were derived from these two timed cohorts. In 2010-2011, 227 sessions were included for the iPhone app validation analysis.

In 2008, the first 4,422 sessions were used for training two primary KIDROP technicians (Level 1). The subsequent 1462 sessions in 2008-09 and 455 sessions by the same technicians upgraded to Level III in 2011-12 were included for kappa correlation and agreement analysis between the technician and ROP expert. The distribution of these 6339 sessions (1601 infants) is summarized in Table 3 and shows that 36.4% of babies had 3 or less imaging sessions before discharge, the remaining (63.6%) had 4 or more sessions.

The distribution of the birth-weight plotted along the gestational age for screened and treated babies is depicted in [Fig. 1] and emphasizes that 28.5% of all infants treated had birth weights of > 1501gm and 6.3% of these 'outliers' had birth weights of > 2000gm.

Table 3: Distribution of 6339 screening sessions by number of episodes

Number of imaging sessions	N=babies	N=sessions	% (babies)
One	38	38	2.4
Two	190	380	11.9
Three	354	1062	22.1
Four	436	1744	27.2
5 or more	583	3115	36.4
Total	1601	6339	100

Table 4: Clinical Utility of Technicians making a diagnosis and calling for follow-up (Level I vs Level III technician)

	2008-2009 (Level I technician) (n=1462)		2011-2012 (Level III technician) (n=454)	
	N	%	N	%
Agreed sessions	1257	85.9	428	94.3
	378 (G); 804 (O); 75 (R)		136 (G); 248 (O); 44 (R)	
Erring towards safety of patient (increases visits)	137	9.4	22	4.8
	72 (SpG, TeO); 65 (SpO, TeR)		10 (SpG, TeO); 12 (SpO, TeR)	
Erring towards possible missed treatment	68	4.7	4	0.9
	13 (SpR, TeO); 55α (SpO, TeG)		2 (SpR, TeO); 2α (SpO, TeG)	

(G: green, O: orange, R: Red, Sp: Specialist, Te: Technician. α None of these infants had any stage of ROP. The disagreement was that the specialist called it avascular in zone 3 and scheduled another visit, while the technician called it mature retina and discharged the patient)

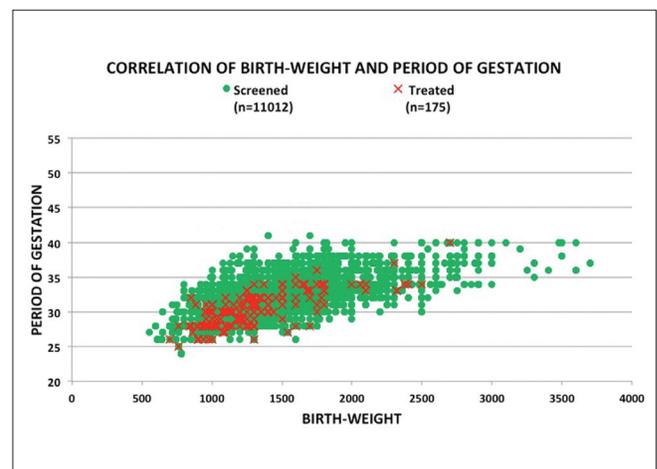


Figure 1: Graphic representation and correlation of birth weight against gestational age of 1601 infants screened and 175 treated

Technician Validation

Level I technicians agreed with 85.9% of all management (red, orange and green) of the expert. This improved to 94.3% of all decisions when they upgraded to Level III. The proportion of sessions where the technicians' management decisions were non-referral when the expert thought this to be indicated dropped from 4.7 to 0.9% (Level I to III). This clinical utility score is summarized in Table 4. Of the 4 infants who were false negatives, two were called 'red' by the specialist and 'orange' ('follow up within a week') by the technician and could have potentially been lost. The other 2 were marked 'orange' (zone 3 avascular) by the specialist and 'green' (mature retina) by the technician and arguably would not acquire 'blinding' disease even if missed. Hence, a Level III technician would miss only 0.4% (and not 0.9%) of infants with treatable lesions. Applying this correction to Level I, only 13 (and not 68 infants) [0.9% (13/1462)] would risk missing treatment.

The sensitivity, specificity, positive predictive value and negative predictive values for diagnosing 'any stage of ROP' and 'treatment grade ROP' during their transition from Level I to III are summarized in Table 5. The discriminatory index [(sensitivity x specificity)/100] improved from 79.5 to 92.7 and 71.6 to 89.2 for 'any stage' and 'treatment grade ROP' respectively. The measurement of agreement (kappa) comparing 1) treatment vs no treatment 2) mild vs severe ROP and 3) discharge vs no discharge is summarized in Table 6, which again demonstrates significant improvement as their skills improved.

iPhone validation

The overall agreement for all 10 categories of diagnoses was 96.3%. The measurement of overall agreement for detecting ROP was kappa 0.96 (SE 0.014, $P < 0.0001$), for type 1 ROP was kappa 0.96, (SE 0.024, $P < 0.0001$) and for mild, Type 2 ROP, was kappa 0.94, (SE 0.037, $P < 0.0001$). The sensitivity, specificity, positive and negative predictive values for severe and mild disease detections are summarized in Table 7.

Discussion

India, like many other middle-income countries is facing the 'third epidemic' of ROP.^[1,2] Over the past two decades, ROP has been reported from major cities of the country with an incidence ranging between 37-54%.^[28-30] Infants blind from ROP continue to present to tertiary level facilities, many of whom have not been screened. Significantly, over the past decade, India has made steady progress in child health care indices and the infant mortality rate (IMR) has dropped from 81/1,000 live births in 1990 to 47/1,000 live births in 2011.^[31] This has led to an increase in surviving neonates, many of whom are preterm, even in rural centers^[7-10] which adds to the unmet challenge of ROP screening compounded by inadequate awareness among pediatricians, gynecologists and lack of sufficiently trained ROP specialists.^[9,16]

Telemedicine for ROP using pediatric wide-field digital retinal imaging with 'remote experts' who grade images is a successful means of bridging this gap.^[2,32] In most 'real-world' programs,^[2] images captured by nurses,^[33-37] ophthalmic

Table 5: Sensitivity and specificity of diagnosis of retinopathy of prematurity: Technician vs specialist (Level I vs Level III technician)

Study period	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)
2008-2009 (Level I Technician)				
Any stage of ROP	94.6 (92.9-95.9)	84.0 (92.9 to 95.9)	93.0 (91.3 to 94.5)	87.3 (83.8 to 90.3)
Treatment grade ROP	85.2 (76.1 to 91.9)	84.0 (80.3 to 87.3)	51.0 (42.7 to 59.4)	96.7 (94.4 to 98.2)
2011-2012 (Level III technician)				
Any stage of ROP	99.4 (97.7 to 99.9)	93.2 (87.8 to 96.7)	96.8 (94.3 to 98.5)	98.6 (94.9 to 99.8)
Treatment grade ROP	95.7 (85.1 to 99.3)	93.2 (87.7 to 96.7)	81.5 (68.6 to 90.7)	98.6 (94.9 to 99.8)

PPV : Positive Predictive Value, NPV : Negative Predictive Value, CI : Confidence Interval, ROP : Retinopathy of Prematurity

Table 6; Measurement of agreement (Kappa) between technician and ROP specialist

	2008-2009				2011-2012			
	Count (total)	Continuity correction	P value	Kappa	Count (total)	Continuity correction	P value	Kappa
Treatment vs no treatment	75 (1462)	609.6	<0.0001	0.63	44 (454)	320.1	<0.0001	0.85
Mild vs severe ROP	75 (957)	380.6	<0.0001	0.61	44 (306)	210.6	<0.0001	0.84
Discharge vs follow-up	957 (1462)	918.6	<0.0001	0.79	306 (454)	396.2	<0.0001	0.94

Table 7: iPhone App Image reading and reporting agreement with Retcam laptop analysis

Study Period	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)
2010-2011 (n=226 sessions)				
Mild ROP	95.5 (84.5 - 99.3)	97.9 (89.1 - 99.7)	97.7 (87.7 - 99.6)	96.0 (86.3 - 99.4)
Treatment grade ROP	98.9 (96.1-99.8)	97.7 (87.7 -99.6)	99.5 (96.9 - 99.9)	95.5 (84.5 - 99.3)

photographers^[38-41] or ophthalmologists^[42-45] are read onsite or remotely by 'ROP experts' using a direct, 'store and forward' or image transfer platforms within a defined time period which could vary from a day to a week. However, in India, finding the 'ROP expert' albeit for remote reading is a huge challenge. With less than 500 registered vitreo-retinal surgeons, it is believed that there are less than 30-35 ROP experts who could provide comprehensive ROP care, and mostly reside in urban areas.

We began KIDROP with the belief that a telemedicine program will not solve our problem unless non-physicians can be trained not only to take images, but also to reliably grade them and make management decisions at the time of image capture. This is particularly important in India where larger, more mature infants develop severe ROP, many of whom have already been discharged from neonatal care. A delay in receiving the management decision from experts would pose an enormous administrative challenge in transmitting the management decision to parents, many of whom are poor, uneducated and who live at a distance from the neonatal center. To our best knowledge, in 2008 this was the first program to train technicians to capture and interpret retinal images.^[2,9-11] We evolved a training and accreditation score (STAT, Table 1) for this purpose. The aim was to provide the mother with a definitive diagnosis and date for the next visit even before she left the neonatal unit. Simultaneously, we tested remote reading by the ROP expert at our headquarters on an indigenously created tele-ROP platform that was enabled on the laptop and smart phone (iPhone) with 'near-live' reporting.

KIDROP was built on a "Triple-T" principle, namely Telemedicine, Training of peripheral ophthalmologists and ophthalmic assistants and Taking the support of neonatologists, pediatricians and gynecologists. The program expanded from 6 pilot districts of Southern Karnataka to 18 districts in all, 12 of these supported by the National Rural Health Mission, Ministry of Health and Family Welfare, Government of Karnataka in the nation's first public private partnership in infant blindness prevention. At the time of submission, 81 neonatal units are serviced by 3 'A' teams and 12 'B' teams (local districts). Over 41,000 screening sessions have been performed using 4 Retcam shuttles and over 860 (10.2% of infants screened) infants have received treatment for ROP.

Previous 'real-world telemedicine programs'^[46] from Canada,^[42] United States,^[34] and Germany^[43] have used trained ophthalmologists or experts to remotely read and interpret images with different terminologies such as referral warranted ROP (RW-ROP)^[42] or clinically significant ROP (CS-ROP)^[34] for

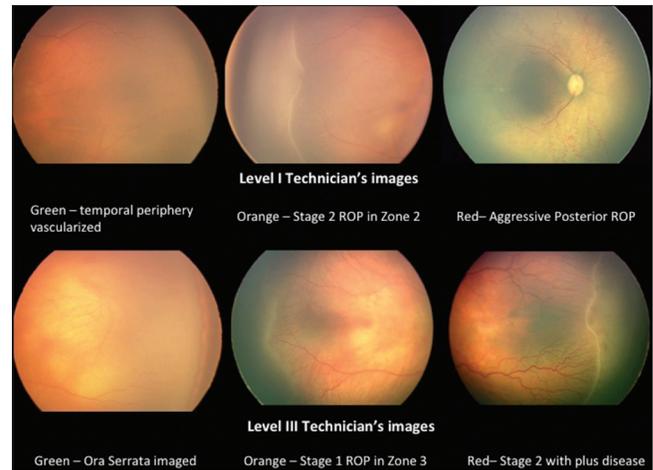


Figure 2: Retcam images captured during Level I technician training (top panel, red, orange and green) and improvement in capturing subtler disease including excellent images of the ora serrata (lower panel, red, orange and green) when they attain Level III status

decision algorithms. We chose a new triage graded protocol based on the new ICROP classification^[25] which places emphasis on the management decision using a colour coding of red, orange and green [Table 2] keeping in mind the nature of demands on a non-physician grader in a remote area. This was conceived so as to create a wider safety net wherein, for example, Type 1 ROP is marked red, stage 1 is followed up (orange) and only mature retina, or definitely regressing ROP is discharged (green) [Fig. 2]. Another layer in the safety net is that no infant in our program is discharged until a mature retina is imaged on two consecutive visits, one of these between 41-45 weeks of postmenstrual age.

Our results demonstrate that Level I technicians have an overall agreement of 85.9% with the expert and this improves to 94.3% when they upgrade to Level III. In our setting, it takes an average of 30 and 90 working days to achieve a skill level of Level I and III respectively. In a screening program of this nature, missing treatable disease could be dangerous, as the child may never have access to a clinical exam by an ROP specialist. Our results show that this occurrence is indeed very low. A Level I technician would miss 0.9% of infants needing treatment and a Level III only 0.4%. The corollary would be the 'false positives', which could add the burden of another visit for the baby and the family. This nearly halves from 9.4% to 4.8% as the skill improves from Level I to III. This can be attributed to their ability to image the temporal periphery up to and including the ora serrata in an increasing proportion of babies, enhancing their confidence of 'discharging' the baby [Fig. 2]. Initially Level I technicians begin by uploading all cases (green, orange and red) for remote expert tele-reporting. With increased expertise, Level III technicians are able to triage better, with the more urgent 'red' cases being uploaded for the ROP specialist to confirm if treatment is required on the live tele-ROP platform. Despite high grades of agreement with the specialist, it is recommended that before a baby is discharged from the screening network, the ROP specialist ratifies this decision by viewing the images or examines the baby on site wherever possible.

In the United Kingdom, under the NHS Diabetic Eye

Screening Programme, technicians from designated central reading centers are employed to interpret downloaded images for diabetic retinopathy changes.^[47] In the KIDROP program, our technicians capture, read and report ROP images 'on-site' and real-time. In future, with increasing volumes of images coming from different parts of the country, central-reading centers may become necessary.

We developed the smart phone app on the iPhone (Apple, CA, USA) for rapid review and reporting. In 2009, this was the first smart phone to provide touch technology, 'pinch and drag', and PDF printing compatibility.^[9,11,19-21] This app allowed the expert anytime access to the images, less dependence on the computer, a user friendly interface to report the diagnosis and suggest follow-up. This is tightly integrated with the database maintained on a cloud-based server and is compliant with regulatory standards. With the proliferation and improvement of smart phone technology, future research would include imaging using the smart phone, App based data management systems and integration with video conferencing.

A limitation of this study program is that it judged the validity of non-physicians to be graders with the assumption that the 'gold standard' for comparison of wide field digital imaging for ROP is dilated indirect ophthalmoscopy. This concept has already been questioned.^[48] Studies suggest that photographic documentation may 'inadvertently' detect mild disease that was 'missed' on ophthalmoscopic examination.^[35] The ability of images to document, review, store and compare disease far outweighs routine indirect ophthalmoscopy, even when performed by an expert. In our country, the current limited expertise to use ophthalmoscopy, particularly in rural areas is a case in favor of non-physician grading. The importance of training and validating the technicians cannot be overemphasized. Another limitation is that the cost-utility of this program has not been formally analyzed. Furthermore, the expertise of other Level III technicians has not been compared against our primary technicians who enjoy over 15,000 sessions each, hence making generalizability an unmeasured entity.

The KIDROP model is now being replicated in two more states and training is completed in two more. Level III technicians are the first line decision makers in the rural periphery who are backed by remote experts who read these images on smart phones. The outcome from these centers is awaited. However, the applicability of this program in other developed countries would attract unaddressed medico-legal constraints and needs evaluation.

In India, as ROP care, awareness, training and expertise among general ophthalmologists and specialists improves, it is likely that there would be less dependence on a program built on the tenants of KIDROP. Until then, the societal impact of missed screening due to lack of trained resources in peripheral areas leading to increased infant blindness would certainly be a factor for considering a 'KIDROP like program' as a model for ROP screening in underserved areas.

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